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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/US92/04891 (22) International Filing Date: 9 June 1992 (09.06.92) (30) Priority data: 716,471 17 June 1991 (17.06.91) US (71) Applicant: SERIM RESEARCH CORPORATION [US/ US]; 23575 County Road 106, Elkhart, IN 46514 (US). (72) Inventors: CHRISTNER, James, Edward ; 1926 Woodland Court, Elkhart, IN 46514 (US). LUCCHESI, Leonard, John, II ; 3221 Calumet Avenue, Elkhart, IN 46514 (US). (74) Agent: STEPHENSON, Harry, T.; 23575 County Road 106, Elkhart, IN 46514 (US).		(81) Designated States: AT (European patent), BE (European patent), CA, CH (European patent), DE (European pa- tent), DK (European patent), ES (European patent), FR (European patent), GB (European patent), GR (Euro- pean patent), IT (European patent), LU (European pa- tent), MC (European patent), NL (European patent), SE (European patent). Published <i>With international search report.</i>
(54) Title: TEST FOR PER ACIDS (57) Abstract A test device and system is disclosed for determining a threshold level of per acid in a solution which may contain peroxide. More specifically the test utilizes a reagent strip format and involves an indicating mechanism for determining if the per acid is at a predetermined critical level or concentration.		

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TEST FOR PER ACIDS

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FIELD OF THE INVENTION

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The present invention involves test systems and devices for the rapid and facile threshold level testing of solutions of per acids in the presence of hydrogen peroxide. More specifically it relates to reagent strip test devices which are capable of giving a response which indicates that the solution being tested, which may also contain hydrogen peroxide, is or is not at a specified level or concentration of per acid.

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BACKGROUND OF THE INVENTION

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Per acids are becoming increasingly important as cold sterilants in such diverse areas as health care and food processing. Because of their chemical nature and how these materials are produced, they are usually quite unstable and exist as combinations of per acid and hydrogen peroxide. For example, peracetic acid can be prepared by allowing acetic acid to react with 30 to 90 percent hydrogen peroxide solution in the presence of sulfuric acid. This reaction is, however, reversible and peroxy acids such as peracetic acid gradually hydrolyze to the corresponding carboxylic acid and hydrogen peroxide. For this reason, when such

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chemicals are used as sterilants, it is absolutely necessary to measure the amount of per acid present to ensure that the proper concentration or level of sterilant is present. This is especially true in the present health care environment which for cost containment reasons encourages reuse of otherwise disposable devices such as dialysis membranes.

One common type of test system or device presently in use in the health care area is the reagent strip. In such a device, the reagent composition which reacts specifically with the analyte of interest to give a colorimetric response is incorporated into a matrix such as paper and a small section of the dried paper is attached to a plastic strip for ease of handling. In use, the reagent strip is immersed momentarily into the solution of analyte and withdrawn. The usual procedure is then to visually compare any color generated in the matrix to a standardized set of color blocks to determine the concentration of analyte in the solution being tested. Such a procedure is quite useful when a wide range of analyte concentrations are encountered in the test samples and each level involves useful information for the analyst.

In the case of sterilants, however, there is usually a relatively exact level of chemical which has been previously determined to be effective and which level must be maintained to ensure that the object or device being treated is in fact sterile after exposure to the cold sterilant. Accordingly, sterilant potency tests are commonly designed to give a so-called "go" or "no go" result. This enables the user to easily determine if the cold sterilant solution has the proper level or concentration of chemical present or if the solution must be either rejuvenated or discarded.

Because of similarities in reactivity between per acids and peroxides, elaborate and cumbersome methods have been devised to assay or measure per acids in the presence of hydrogen peroxide. Such methods usually rely on removal of the peroxide prior to determining the per acid or utilizing differences between per acid and peroxide in the speed of reaction of the test reagent therewith. For example, schemes are utilized which involve cooling the sample solution down to between 0 to 5 °C prior to adding the test reagents. This cooling step then allows the determination of per acid in the presence of peroxide.

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DESCRIPTION OF THE PRIOR ART

Sully, B. D. and Williams, P. L., Analyst, 1962, 87, 653 describe a liquid method for the determination of per-acids in the presence of hydrogen peroxide. Basically the method involves adding excess potassium iodide to a sample solution of per acid and hydrogen peroxide cooled down to less than 5 °C. The iodine liberated by the per acid is then titrated with 0.1 N sodium thiosulfate with starch as an indicator. This portion of the procedure which involves the determination of per acid relies on the fact that per acids react much more rapidly than hydrogen peroxide at a temperature of less than 5 °C. A second step is then used to determine the peroxide present in the test sample. The paper also gives a background discussion relative to per acid analyses and cites relevant literature references.

SUMMARY OF THE INVENTION

The present invention relates to reagent strip test devices which are set to give a colorimetric response to a predetermined level of per acid in the presence of hydrogen peroxide. The method of analysis is rapid and facile and does not involve temperature controls. More specifically, the reagent strip test devices described herein involve the following test composition incorporated into a matrix: a water soluble iodide in a quantity in excess of that required to react with the per acid present to generate iodine, a predetermined amount of a water soluble thiosulfate which reacts with the iodine generated and which amount depends on the level of peracid being detected and preferably an indicator which responds to any iodine in excess of that reacting with the thiosulfate. The preferred reagent strip matrix is paper and the preferred indicator is soluble starch.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The analytes of the present invention are per acids which may be described by the following structure:



where R is hydrogen, methyl, ethyl, phenyl, carboxyphenyl and furan. Examples of such per acids are: peroxyformic acid, peroxyacetic acid,

peroxyphthalic acid, peroxybenzoic acid,
peroxypropionic acid and peroxyfuroic acid.

Referring now to the reagent composition of the
5 present invention, water soluble components are usually
preferred since impregnation into the supporting matrix
is thereby facilitated. As the source of iodide, any
water soluble iodide can be employed with the
preferable materials being potassium or sodium iodide.
10 The water soluble thiosulfate may be any of a variety
of materials which when dissolved release the
thiosulfate ion. Potassium thiosulfate is the
preferred compound because of its availability and
cost. Although the excess iodine generated may be
15 detected directly by its characteristic brown color,
it is preferable to add an indicator to the test
composition. The indicators of the present invention
are any of a variety of materials which respond to the
presence of iodine in solution to give a colorimetric
20 response, with the understanding that black is included
as a color. Examples of indicators are starch such as
Thyodene (a partially hydrolyzed starch) and
polyvinylpyrrolidone may be used with soluble starch
the preferred material.

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The compositions described herein are incorporated
into a matrix to give the reagent strip format. The
matrix is usually a flat, thin sheet-like material
which is used to contain the test composition and allow
30 the test solution containing the analyte to contact and
react with the reagent system. By "incorporation" it
is meant that the composition is either impregnated
into a preformed matrix and dried or is mixed into a
liquid polymeric material and cast as a film and dried
35 to form the matrix. The preformed matrix materials
commonly used are paper or cellulosic materials, glass

fibers and either woven or non-woven synthetic fibrous materials. The polymeric matrices are made from a variety of polymers which when cast as a film are porous and allow the fluid being tested to penetrate the matrix and react with the test composition. When such a polymeric matrix is used, it is common practice to mix the test reagent composition with the liquid polymer prior to film formation. Alternatively, the matrix may comprise attaching the test composition either chemically or physically to polymeric beads or granules and supporting the resultant materials on a support.

After incorporating the test composition into a matrix, the matrix is preferably attached to a support usually consisting of a plastic sheet material such as polystyrene which allows the user to immerse the matrix containing the test reagent composition into the test fluid for a predetermined period of time, withdrawing it and comparing the color formed to a standardized chart for comparison purposes. Alternatively, if the color change is distinct enough, such as when it changes from white to black, the color chart may be omitted.

Except for the concentration of the thiosulfate in the test reagent mix, there is a wide latitude of ingredient concentrations which may be used to prepare the test reagent compositions of the present invention. Basically the iodide should be present in a range of concentrations of about from 2.2 grams per liter to 9.0 grams per liter and, if an indicator is used, it should be present in an amount sufficient to give the desired visual response. A buffer may also be advantageously used to keep the pH of the test composition in a range of about from 3 to 7. Representative of such buffers

which may be used are citrate, acetate, phosphate, succinate and formate, with citrate a preferable buffer.

5 The thiosulfate concentration in the test composition is adjusted such that the iodine released from the reaction of the per acid with the iodide is consumed unless the concentration of the per acid is at a predetermined minimum level or concentration. In
10 such an event the excess iodine is either detected by its characteristic color or causes the indicator to respond indicating that the sterilant is present in a quantity sufficient to effect the desired sterilizing result. Accordingly, the thiosulfate concentration is
15 adjusted to reflect the level of per acid being determined. Basically the concentration of thiosulfate with respect to per acid is set as follows: since one gram-molecular weight (mole) of per acid reacts with iodide to form one mole of iodine which in turn
20 oxidizes two moles of thiosulfate, the thiosulfate must be present in a molar concentration twice that of the amount of per acid to be detected.

 When the test composition of the present invention
25 is contacted with a solution of per acid and peroxide, it has surprisingly been found that, at room temperature, the per acid reaction proceeds rapidly in comparison to the peroxide reaction so that there is no need to cool the test composition and test fluid to
30 that required by the prior art, i. e. 0 to 5 °C. This is extremely advantageous since it allows the on-site testing of sterilant fluids and does not require a laboratory setting accompanied by the delays and costs associated therewith.

EXAMPLE

5 A sheet of Whatman #54 absorbant filter paper was
saturated with a solution of the following ingredients:
5.0 grams sodium thiosulfate, 4.5 grams potassium
iodide, 22.6 grams ammonium citrate, 250.0 ml 1%
soluble starch solution and 750.0 ml distilled water.
The saturated paper was dried at 65 °C for 15 minutes
10 and cut into one fifth inch squares. The square
reagent pads were then attached to the end of three by
one-fifth inch strips of transparent sheet material
which acted as handles for the test devices. When the
reagent strip test pad areas were dipped into a
15 solution of 800 ppm peracetic acid (PAA) at 20 °C, the
pad immediately changed from white to a dark blue
color. When additional strips were dipped into a
solution of 500 ppm PAA, no color formed. In both
instances, 1.0% peroxide was present which did not
20 interfere with the PAA test results.

What is claimed is:

1. A test device for detecting a predetermined
5 threshold level of a per acid in an aqueous sample solution
comprising a matrix material incorporating the dried residue
of test composition which comprises:
 - a. a water soluble iodide in a quantity in excess of
the required to react with all of the per acid present in
10 the sample solution to form iodine; and
 - b. a predetermined limited quantity of a water soluble
thiosulfate said quantity being dependent upon the level of
per acid being detected.
- 15 2. A test device as recited in Claim 1 wherein the
test composition includes a colorimetric indicator
responsive to any excess iodine after completion of the
reaction of the thiosulfate present with the iodine formed.
- 20 3. A test device as recited in claim 2 wherein the
indicator is starch.
4. A test device as recited in claim 1 wherein the
matrix material is absorbant paper.
- 25 5. A test device as recited in claim 1 wherein the per
acid being detected is peroxyacetic acid.
6. A method for detecting a predetermined threshold
30 level of per acid in an aqueous sample solution comprising
contacting the sample solution with a test reagent
composition comprising a quantity of water soluble iodide in
excess of that required to react with all of the per acid
present in the sample solution, and a predetermined limited
35 quantity of a water soluble thiosulfate, said quantity being

dependent upon the level of per acid being detected and thereafter observing the presence of excess iodine.

5 7. A method as recited in claim 6 wherein a colorimetric indicator is used to determine the presence of excess iodine.

10 8. A method as recited in claim 7 wherein the indicator is starch.

9. A method as recited in claim 6 wherein the reagent composition is incorporated in a matrix material and the matrix is presented to the sample solution.

15 10. A method as recited in claim 9 wherein the matrix material is absorbant paper.

11. A method as in claim 6 wherein the per acid being detected is peroxyacetic acid.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US92/04891

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) : G01N 21/77, 31/22

US CL : 422/56: 436/129, 135, 169

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 422/56; 436/129, 135, 169

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS

search terms: peracid, peroxy acid, peroxyacetic acid, thiosulfate, iodine, iodide, starch, peroxide

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X — Y	US, A, 3,121,615 (Price) 18 February 1964, col. 2, line 34 to col. 3, line 18.	1,4,5 — 2,3,6-11
Y	US, A, 4,098,575, (Matsushita) 04 July 1978, see entire document.	1-11
Y	US, A, 4,900,682, (Fischer et al.) 13 February 1990, see entire document.	1-11
Y	Feigl et al., "Spot Tests in Organic Analysis", published 1966 by Elsevier Scientific Publishing Company: New York, page 615.	1-11
A	US, A, 3,183,173 (Oakes) 11 May 1965.	1-11
A	US, A, 3,814,668 (Blake et al.) 04 June 1974.	1-11
A	US, A, 4,303,753 (Lam) 01 December 1981.	1-11
A	SU, A, 253,426 (Shapilov OD Kostyukovskii YaL.) 27 February 1970.	1-11
A	Treadwell, F. P., "Analytical Chemistry" vol. 1, published 1930 by John Wiley & Sons, Inc.: New York, pp. 89-90.	1-11



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:	*T	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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International application No.
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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Swoboda et al., "Determination of the Peroxide Value of Edible Fats by Colorimetric Iodometric Procedures", published 1959 by Chem. & Industry, pages 1090-91.	1-11
A	Daniel Swern, Ed., "Organic Peroxides", published 1970 by Wiley-Interscience: New York, pp. 369,461,464,468,497-516.	1-11